

In the Specification

Page 7, line 18, immediately prior to "three-plasmid", insert --prior art--.

In the Claims

Please amend Claims 1, 5, 7, 8, 12, 16, 20, 22, 23, 27, 31 and 35 as follows:

- D1
B1
1. (Amended) A packaging cell line [for producing a viral accessory protein independent HIV-derived retroviral vector particle] comprising:
- a) a mammalian cell;
 - b) a first retroviral nucleotide sequence in the cell which comprises a codon optimized coding sequence for a HIV *gagpol*[, wherein said coding sequence has been mutagenized to improve expression of the HIV *gagpol* proteins] but not coding sequences for HIV accessory proteins or constitutive transport elements;
 - c) a second retroviral nucleotide sequence in the cell which comprises the coding sequence for a heterologous envelope protein; and
 - d) a third retroviral nucleotide sequence in the cell which comprises a DNA sequence of interest and HIV cis-acting sequences required for packaging, reverse transcription and integration,
- wherein said packaging cell line produces a HIV-derived retroviral vector particle.

- D2
B2
5. (Amended) A packaging cell line comprising:
- a) a mammalian cell;
 - b) a first retroviral nucleotide sequence in the cell which comprises a codon optimized coding sequence for a HIV *gagpol*[, wherein said coding sequence has been mutagenized to improve expression of the HIV *gagpol* proteins] but not coding sequences for HIV accessory proteins or constitutive transport elements; and
 - c) a second retroviral nucleotide sequence in the cell which comprises a DNA sequence of interest and HIV cis-acting sequences required for packaging, reverse transcription and integration.

- B3
D3
7. (Amended) A packaging cell line comprising:

- DB
cont
- a) a mammalian cell;
 - b) a first retroviral nucleotide sequence in the cell which comprises a codon optimized coding sequence for a HIV *gagpol*[, wherein said coding sequence has been mutagenized to improve expression of the HIV *gagpol* proteins] but not coding sequences for HIV accessory proteins or constitutive transport elements; and
 - c) a second retroviral nucleotide sequence in the cell which comprises the coding sequence for a heterologous envelope protein.

DB
cont

8. (Amended) A method of producing a packaging cell line which produces [for producing] a [viral accessory protein independent] HIV-derived retroviral vector particle, comprising co-transfecting mammalian host cells with:

- a) a first plasmid comprising a codon optimized DNA sequence which encodes HIV *gagpol* proteins[, wherein said DNA sequence has been mutagenized to improve expression of the HIV *gag* and *pol* proteins] but not DNA sequences encoding HIV accessory proteins or constitutive transport elements;
- b) a second plasmid comprising a DNA sequence which encodes a heterologous envelope protein; and
- c) a third plasmid comprising a DNA sequence of interest and HIV cis-acting sequences required for packaging, reverse transcription and integration, thereby producing a packaging cell line which produces a HIV-derived retroviral vector particle.

Sub
C1
B4

12. (Amended) A method of producing a [viral accessory protein independent] HIV-derived retroviral vector particle comprising co-transfecting mammalian host cells with:

- a) a first plasmid comprising a codon optimized DNA sequence which encodes HIV *gagpol* proteins[, wherein said DNA sequence has been mutagenized to improve expression of the HIV *gagpol* proteins] but not DNA sequences encoding HIV accessory proteins or constitutive transport elements;
- b) a second plasmid comprising a DNA sequence which encodes a heterologous envelope protein; and

B4
Cont. art. 101

a third plasmid comprising a DNA sequence of interest and HIV cis-acting sequences required for packaging, reverse transcription and integration, thereby producing a HIV-derived retroviral particle.

16. (Amended) A packaging cell line [for producing a viral accessory protein independent lentivirus-derived retroviral vector particle] comprising:
- a) a mammalian cell;
 - b) a first retroviral nucleotide sequence in the cell which comprises a codon optimized coding sequence for a lentivirus *gagpol*[, wherein said coding sequence has been mutagenized to improve expression of the lentivirus *gagpol* proteins] but not coding sequences for lentivirus accessory proteins or constitutive transport elements;
 - c) a second retroviral nucleotide sequence in the cell which comprises the coding sequence for a heterologous envelope protein; and
 - d) a third retroviral nucleotide sequence in the cell which comprises a DNA sequence of interest and lentivirus cis-acting sequences required for packaging, reverse transcription and integration,
- wherein said packaging cell line produces a lentivirus-derived retroviral vector particle.

20. (Amended) A packaging cell line comprising:
- a) a mammalian cell;
 - b) a first retroviral nucleotide sequence in the cell which comprises a codon optimized coding sequence for lentivirus *gagpol*[, wherein said coding sequence has been mutagenized to improve expression of the lentivirus *gagpol* proteins] but not coding sequences for lentivirus accessory proteins or constitutive transport elements; and
 - c) a second retroviral nucleotide sequence in the cell which comprises a DNA sequence of interest and lentivirus cis-acting sequences required for packaging, reverse transcription and integration.

22. (Amended) A packaging cell line comprising:

- a) a mammalian cell;

- b) a first retroviral nucleotide sequence in the cell which comprises a codon optimized coding sequence for lentivirus *gagpol*[, wherein said coding sequence has been mutagenized to improve expression of the lentivirus *gagpol* proteins] but not coding sequences for lentivirus accessory proteins or constitutive transport elements; and
- c) a second retroviral nucleotide sequence in the cell which comprises the coding sequence for a heterologous envelope protein.

23. (Amended) A method of producing a packaging cell line which produces [for producing] a [viral accessory protein independent] lentivirus-derived retroviral vector particle, comprising co-transfecting mammalian host cells with:

- a) a first plasmid comprising a codon optimized DNA sequence which encodes lentivirus *gagpol* proteins[, wherein said DNA sequence has been mutagenized to improve expression of the lentivirus *gag* and *pol* proteins] but not DNA sequences encoding lentivirus accessory proteins or constitutive transport elements;
- b) a second plasmid comprising a DNA sequence which encodes a heterologous envelope protein; and
- c) a third plasmid comprising a DNA sequence of interest and lentivirus cis-acting sequences required for packaging, reverse transcription and integration, thereby producing a packaging cell line which produces a lentivirus-derived retroviral vector particle.

27. (Amended) A method of producing a [viral accessory protein independent] lentivirus-derived retroviral vector particle comprising co-transfecting mammalian host cells with:
- a) a first plasmid comprising a codon optimized DNA sequence which encodes lentivirus *gagpol* proteins[, wherein said DNA sequence has been mutagenized to improve expression of the lentivirus *gagpol* proteins] but not DNA sequences encoding lentivirus accessory proteins or constitutive transport elements;
 - b) a second plasmid comprising a DNA sequence which encodes a heterologous envelope protein; and
 - c) a third plasmid comprising a DNA sequence of interest and lentivirus cis-acting sequences required for packaging, reverse transcription and integration,

Sub C2 B8 cont. Cont.
thereby producing a lentivirus-derived retroviral vector particle.

- Sub C3 B9*
31. (Amended) A [viral accessory protein independent] HIV-derived retroviral vector particle having no viral accessory proteins produced by the method comprising co-transfecting mammalian host cells with:
- a) a first plasmid comprising a codon optimized DNA sequence which encodes HIV *gagpol* proteins[, wherein said DNA sequence has been mutagenized to improve expression of the HIV *gagpol* proteins] but not DNA sequences encoding HIV accessory proteins or constitutive transport elements;
 - b) a second plasmid comprising a DNA sequence which encodes a heterologous envelope protein; and
 - c) a third plasmid comprising a DNA sequence of interest and HIV cis-acting sequences required for packaging, reverse transcription and integration.

- Sub C5 B10*
35. (Amended) A [viral accessory protein independent] lentivirus-derived retroviral vector particle having no viral accessory proteins, produced by the method comprising co-transfecting mammalian host cells with:
- a) a first plasmid comprising a codon optimized DNA sequence which encodes lentivirus *gagpol* proteins[, wherein said DNA sequence has been mutagenized to improve expression of the lentivirus *gagpol* proteins] but not DNA sequences encoding lentivirus accessory proteins or constitutive transport elements;
 - b) a second plasmid comprising a DNA sequence which encodes a heterologous envelope protein; and
 - c) a third plasmid comprising a DNA sequence of interest and lentivirus cis-acting sequences required for packaging, reverse transcription and integration.

REMARKS

Specification Amendment

The specification has been amended to more clearly recite that the three-plasmid expression system described in Naldini *et al.*, *Science*, 272:263-267 (1996), and shown